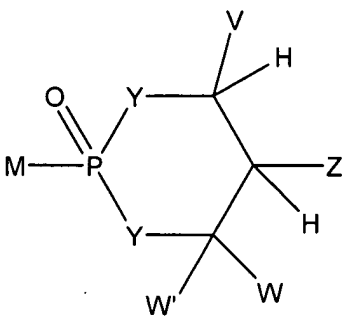


In the claims:

Please amend the claims as indicated below. A complete set of all claims previously submitted, including the status for each claim, immediately follows below.

1. (Original) A compound of formula I:



I

wherein:

V, W, and W' are independently selected from the group of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxy carbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxy carbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group of $-\text{CHR}^2\text{OH}$, $-\text{CHR}^2\text{OC}(\text{O})\text{R}^3$, $-\text{CHR}^2\text{OC}(\text{S})\text{R}^3$, $-\text{CHR}^2\text{OC}(\text{S})\text{OR}^3$, $-\text{CHR}^2\text{OC}(\text{O})\text{SR}^3$, $-\text{CHR}^2\text{OCO}_2\text{R}^3$, $-\text{OR}^2$, $-\text{SR}^2$, $-\text{CHR}^2\text{N}_3$, $-\text{CH}_2\text{aryl}$, $-\text{CH}(\text{aryl})\text{OH}$, $-\text{CH}(\text{CH}=\text{CR}^2_2)\text{OH}$, $-\text{CH}(\text{C}\equiv\text{CR}^2)\text{OH}$, $-\text{R}^2$, $-\text{NR}^2_2$, $-\text{OCOR}^3$, $-\text{OCO}_2\text{R}^3$, $-\text{SCOR}^3$, $-\text{SCO}_2\text{R}^3$, $-\text{NHCOR}^2$, $-\text{NHCO}_2\text{R}^3$, $-\text{CH}_2\text{NHaryl}$, $-(\text{CH}_2)_p\text{-OR}^{12}$, and $-(\text{CH}_2)_p\text{-SR}^{12}$;

p is an integer 2 or 3;

with the provisos that:

- a) V, Z, W, W' are not all -H;
- b) when Z is $-\text{R}^2$ or $-\text{OR}^2$, then V is not -H, alkyl, aralkyl, or alicyclic;
- c) when Z is CHR^2OH , then M is not $-\text{NH}(\text{lower alkyl})$, $-\text{N}(\text{lower alkyl})_2$, $-\text{NH}(\text{lower alkylhalide})$, $-\text{N}(\text{lower alkylhalide})_2$ or $-\text{N}(\text{lower alkyl})(\text{lower alkylhalide})$; and
- d) when V is aryl or substituted aryl, then M is not $-\text{O}(\text{D})$ where D is hydrogen, a metal ion or an ammonium ion;

R^2 is selected from the group of R^3 and -H;

R^3 is selected from the group of alkyl, aryl, alicyclic, and aralkyl;

R^6 is selected from the group of -H, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

R^{12} is selected from the group of -H, and lower acyl;

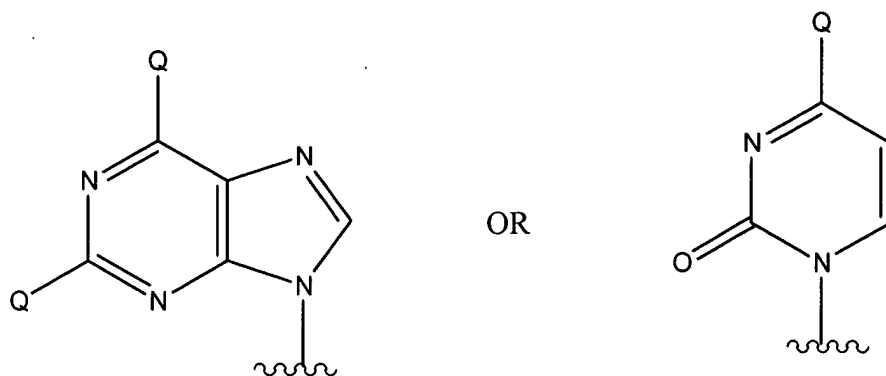
each Y is independently selected from the group of -O-, and $-\text{NR}^6$ -;

M is selected from the group of drugs MH containing an -OH, $-\text{NHR}^2$, or -SH group, and that is attached to the phosphorus in formula I via O, N, or S of said OH, $-\text{NHR}^2$, or SH group;

and pharmaceutically acceptable prodrugs and salts thereof.

2. (Original) A compound according to claim 1, with the further proviso that when Z is CHR^2OH and V, W, and W' are H, then M does not include within its structure adenine,

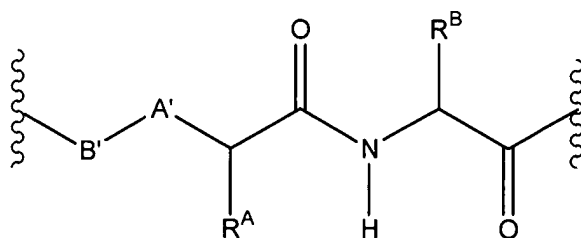
cytosine, guanine, thymine, uracil, 2,6-diamino purine, hypoxanthine, or a compound of the formula:



wherein Q is independently H, Cl, NHR^Q , NR^Q_2 , NHC(O)R^Q , $\text{N(C(O)R}^Q)_2$, OH or $\text{NCHN(R}^Q)_2$; and

R^Q is C_1 - C_{20} alkyl, aryl or aralkyl all optionally substituted with hydroxy or halogen.

3. (Original) A compound according claim 1, with the further proviso that when Z, W, and W' are H and V is aryl, substituted aryl, heteroaryl or substituted heteroaryl, then M does not include within its structure a group of the following formula:



wherein:

R^A and R^B are independently hydrogen, optionally substituted alkyl having from 1 to about 14 carbons, or optionally substituted cycloalkyl having from 3 to about 10 carbons;

A' is NH or $(\text{CH}_2)_k$ where k is an integer from 0 to 3; and

B' is carbonyl or SO_2 .

4. (Original) A compound according to claim 1 wherein MH is selected from the group of antiviral, anticancer, antihyperlipidemic, anti-inflammatory, antifibrotic, anti-diabetic and antiparasitic agents, with the proviso that said anti-diabetic agent is not an FBPase inhibitor.

5. (Original) A compound according to claim 4 wherein MH is selected from the group of etoposide, teniposide, NK-611, GL-331, camptothecin, irinotecan, 9-aminocamptothecin, GG-211, topotecan, lurtotecan, DX-8951F, SKF 107874, SKF 108025, docetaxel, FCE-28161, paclitaxel, mitoxantrone, combretastatin A-4, Azatoxin, mycophenolic acid, coformycin, deoxycoformycin, S,S-dioxolane Combretastatin A-4, doxorubicin, daunorubicin, idarubicin, epirubicin, pirarubicin, mitomycin, eflornithine, piroxantrone, mitoxantrone, neocarzinostatin, esperamicin, calicheamicin theta, and losoxantrone.

6. (Original) A compound according to claim 5 wherein MH is selected from the group of etoposide, teniposide, doxorubicin, pirarubicin, mitoxantrone, topotecan, irinotecan, combretastatin A-4, S,S-dioxolane combretastatin, neocarzinostatin, and calicheamicin.

7. (Original) A compound according to claim 1 wherein at least one Y group is -O-.

8. (Original) A compound according to claim 7 wherein both Y groups are -O-, or when one Y group is -O-, then it is located closest to the W' and W groups.

9. (Original) A compound according to claim 8 wherein both Y groups are -O-.

10. (Original) A compound according to claim 1 wherein
V is selected from the group of aryl, substituted aryl, heteroaryl, and substituted heteroaryl;

W, and W' are independently selected from the group of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxy carbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus; or

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom; or

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms.

11. (Original) A compound according to claim 1, wherein

V, W and W' are independently selected from the group of aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl and 1-alkynyl, and Z is selected from the group of -OR², -SR², -R², -NR²₂, -OCOR³, -OCO₂R³, -SCOR³, -SCO₂R³, -NHCOR², -NHCO₂R³, -(CH₂)_p-OR¹², and -(CH₂)_p-SR¹²; or

V, W, and W' are independently selected from the group of H, alkyl, aralkyl and alicyclic, and Z is selected from the group of -CHR²OH, -CHR²OC(O)R³, -CHR²OC(S)R³, -CHR²OCO₂R³, -CHR²OC(O)SR³, -CHR²OC(S)OR³, -SR², -CH₂aryl, -CH(aryl)OH, -CH(CH=CR²₂)OH, -CH(C≡CR²)OH; and -CH₂NHaryl; or

together V and W are connected via an additional 3 carbon atoms to form a cyclic substituted group containing 6 carbon atoms and mono-substituted with a substituent selected from the group of hydroxyl, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxy carbonyloxy attached to one of said additional carbon atoms that is three atoms from an Y attached to the phosphorus.

12. (Original) A compound according to claim 11, wherein V is selected from the group of aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl and 1-alkynyl, and Z is selected from the group of -OR², -SR², -R², -NR²₂, -OCOR³, -OCO₂R³, -SCOR³, -SCO₂R³, -NHCOR², -NHCO₂R³, -(CH₂)_p-OR¹², and -(CH₂)_p-SR¹².

13. (Original) A compound according to claim 11, wherein V, W and W' are independently selected from the group of H, alkyl, aralkyl and alicyclic, and Z is selected from the group of -CHR²OH, -CHR²OC(O)R³, -CHR²OC(S)R³, -CHR²OCO₂R³, -CHR²OC(O)SR³, -CHR²OC(S)OR³, -SR², -CH₂aryl, -CH(aryl)OH, -CH(CH=CR²₂)OH, -CH(C≡CR²)OH; and -CH₂NHaryl.

14. (Original) A compound according to claim 11, wherein together V and W are connected via an additional 3 carbon atoms to form a cyclic group containing 6 carbon atoms and mono-substituted with a substituent selected from the group of hydroxyl, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy attached to one of said additional carbon atoms that is three atoms from an Y attached to the phosphorus.

15. (Original) A compound according to claim 12 wherein Z, W, and W' are H; and R⁶ is selected from the group of -H and lower alkyl.

16. (Original) A compound according to claim 15 wherein V is selected from the group of aryl and substituted aryl.

17. (Original) A compound according to claim 16 wherein V is selected from the group of phenyl and substituted phenyl.

18. (Original) A compound according to claim 17 wherein V is selected from the group of phenyl, 3,5-dichlorophenyl, 3-bromo-4-fluorophenyl, 3-chlorophenyl, 2-bromophenyl, and 3-bromophenyl.

19. (Original) A compound according to claim 15 wherein V is selected from the group of heteroaryl and substituted heteroaryl.

20. (Original) A compound according to claim 19 wherein V is 4-pyridyl.

21. (Original) A compound according to claim 1 wherein together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, that is fused to an aryl group at the beta and gamma positions to the Y attached to phosphorus.

22. (Original) A compound according to claim 21 wherein said aryl group is an optionally substituted monocyclic aryl group and the connection between Z and the aryl group is selected from the group of O, CH₂, CH₂CH₂, OCH₂ or CH₂O.

23. (Original) A compound according to claim 11 wherein together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and mono-substituted with one substituent selected from the group of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy attached to one of said additional carbon atoms that is three atoms from an Y attached to the phosphorus.

24. (Original) A compound according to claim 23 wherein together V and W form a cyclic group selected from the group of $-\text{CH}_2\text{-CH}(\text{OH})\text{-CH}_2-$, $-\text{CH}_2\text{CH}(\text{OCOR}^3)\text{-CH}_2-$, and $-\text{CH}_2\text{CH}(\text{OCO}_2\text{R}^3)\text{-CH}_2-$.

25. (Original) A compound according to claim 13 wherein W, W' and V are $-\text{H}$.

26. (Original) A compound according to claim 12 wherein Z is selected from the group of $-\text{OR}^2$, $-\text{R}^2$, $-\text{OCOR}^3$, $-\text{OCO}_2\text{R}^3$, $-\text{NHCOR}^2$, $-(\text{CH}_2)_p\text{-OR}^{12}$, and $-(\text{CH}_2)_p\text{-SR}^{12}$.

27. (Original) A compound according to claim 26 wherein Z is selected from the group of $-\text{OR}^2$, $-\text{R}^2$, $-\text{OCOR}^3$, $-\text{OCO}_2\text{R}^3$, and $-\text{NHCOR}^2$.

28. (Original) A compound according to claim 27 wherein Z is selected from the group of H and lower alkyl.

29. (Original) A compound according to claim 10 wherein W and W' are independently selected from the group of H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl and 1-alkynyl.

30. (Original) A compound according to claim 29 wherein W and W' are the same group.

31. (Original) A compound according to claim 30 wherein W and W' are H.

32. (Original) A compound according to claim 12 wherein M is attached to phosphorus via an oxygen or nitrogen atom.

33. (Original) A compound according to claim 32 wherein V is selected from the group of aryl and substituted aryl.

34. (Original) A compound according to claim 33 wherein V is selected from the group of phenyl, 3,5-dichlorophenyl, 3-bromo-4-fluorophenyl, 3-chlorophenyl, 2-bromophenyl, and 3-bromophenyl.

35. (Original) A compound according to claim 32 wherein V is selected from the group of heteroaryl and substituted heteroaryl.

36. (Original) A compound according to claim 35 wherein V is 4-pyridyl.

37. (Original) A compound according to claim 13 wherein M is attached to the phosphorus via a nitrogen or oxygen atom.

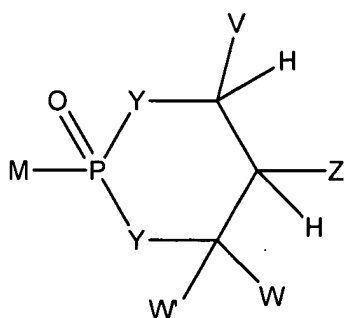
38. (Original) A compound according to claim 37 wherein Z is selected from the group of $-\text{CHR}^2\text{OH}$, $-\text{CHR}^2\text{OC}(\text{O})\text{R}^3$, and $-\text{CHR}^2\text{OCO}_2\text{R}^3$, and wherein R^2 is H or aryl.

39. (Original) A compound according to claim 38 wherein R^2 is -H.

40. (Original) A compound according to claim 12 wherein W' and Z are -H, W and V are both the same aryl, substituted aryl, heteroaryl, or substituted heteroaryl, and V and W are cis to each other.

41. (Original) A compound according to claim 12 wherein W and W' are H, V is selected from the group of aryl, substituted aryl, heteroaryl, substituted heteroaryl, and Z is selected from the group of -H, OR^2 , and $-\text{NHCOR}^2$.

42. (Original) A compound according to claim 41 wherein Z is -H.
43. (Original) A compound according to claim 42 wherein V is selected from the group of phenyl and substituted phenyl.
44. (Original) A compound according to claim 42 wherein V is an optionally substituted monocyclic heteroaryl containing at least one nitrogen atom.
45. (Original) A compound according to claim 44 wherein V is 4-pyridyl.
46. (Original) A compound according to claim 41 wherein V is selected from the group of phenyl, phenyl substituted with 1-3 halogens, and 4-pyridyl and MH is selected from the group of etoposide, doxorubicin, and taxol.
47. (Original) A compound according to claim 42 wherein M is attached to the phosphorus via an oxygen atom.
48. (Original) A compound according to claim 1 wherein MH is from the class epipodophyllotoxins.
49. (Original) A compound according to claim 48 wherein MH is selected from the group of Etoposide, Teniposide, NK-611, GL-331, and Azatoxin.
- 50.-64. (Withdrawn)
65. (Original) A compound of formula I:



wherein

W and W' are independently selected from the group of -H, alkyl, aryl, substituted aryl, heteroaryl, and substituted heteroaryl;

V is selected from the group of aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl and 1-alkynyl;

Z is selected from the group of $-OR^2$, $-SR^2$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) when V is aryl or substituted aryl, then M is not $-O(D)$ where D is hydrogen, a metal ion or an ammonium ion; and

b) when Z is CHR^2OH , then M is not $-NH(\text{lower alkyl})$, $-N(\text{lower alkyl})_2$, $-NH(\text{lower alkylhalide})$, $-N(\text{lower alkylhalide})_2$ or $-N(\text{lower alkyl})(\text{lower alkylhalide})$;

R^2 is selected from the group of R^3 and -H;

R^3 is selected from the group of alkyl, aryl, alicyclic, and aralkyl;

R^6 is selected from the group of -H, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

R^{12} is selected from the group of -H, and lower acyl;

each Y is independently selected from the group of $-O-$, and $-NR^6-$;

M is selected from the group of drugs MH having an -OH, $-NHR^2$, or -SH group, and that is attached to the phosphorus in formula I via O, N, or S of said OH, $-NHR^2$, or SH group;

and pharmaceutically acceptable prodrugs and salts thereof.

66. (Original) A compound according to claim 65 wherein MH is selected from the group of antiviral, anticancer, antihyperlipidemic, anti-inflammatory, antifibrotic, anti-diabetic and antiparasitic agents, with the proviso that said anti-diabetic agent is not an FBPase inhibitor.

67. (Original) A compound according to claim 66 wherein MH is selected from the group of etoposide, teniposide, NK-611, GL-331, camptothecin, irinotecan, 9-aminocamptothecin, GG-211, topotecan, lurtotecan, DX-8951F, SKF 107874, SKF 108025, docetaxel, FCE-28161, paclitaxel, mitoxantrone, combretastatin A-4, Azatoxin, mycophenolic acid, coformycin, deoxycoformycin, S,S-dioxolane Combretastatin A-4, doxorubicin, daunorubicin, idarubicin, epirubicin, pirarubicin, mitomycin, eflornithine, piroxantrone, mitoxantrone, neocarzinostatin, esperamicin, calicheamicin theta, and losoxantrone.

68. (Original) A compound according to claim 67 wherein MH is selected from the group of etoposide, teniposide, doxorubicin, pirarubicin, mitoxantrone, topotecan, irinotecan, combretastatin A-4, S,S-dioxolane combretastatin, neocarzinostatin, and calicheamicin.

69. (Original) A compound according to claim 65 wherein at least one Y group is -O-.

70. (Original) A compound according to claim 69 wherein both Y groups are -O-, or when one Y group is -O-, then it is located closest to the W' and W groups.

71. (Original) A compound according to claim 70 wherein both Y groups are -O-.

72. (Original) A compound according to claim 71 wherein Z, W, and W' are H; and V is selected from the group of aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

73. (Original) A compound according to claim 65 wherein Z, W, and W' are H; and R⁶ is selected from the group of -H and lower alkyl.

74. (Original) A compound according to claim 73 wherein V is selected from the group of aryl and substituted aryl.

75. (Original) A compound according to claim 74 wherein V is selected from the group of phenyl, 3,5-dichlorophenyl, 3-bromo-4-fluorophenyl, 3-chlorophenyl, 2-bromophenyl, and 3-bromophenyl.

76. (Original) A compound according to claim 73 wherein V is selected from the group of heteroaryl and substituted heteroaryl.

77. (Original) A compound according to claim 76 wherein V is 4-pyridyl.

78. (Original) A compound according to claim 65 wherein Z is selected from the group of $-OR^2$, $-R^2$, $-OCOR^3$, $-OCO_2R^3$, $-NHCOR^2$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$.

79. (Original) A compound according to claim 65 wherein W and W' are the same group.

80. (Original) A compound according to claim 79 wherein Z, W, and W' are H.

81. (Original) A compound according to claim 66 wherein M is attached to phosphorus via an oxygen or nitrogen atom.

82. (Original) A compound according to claim 81 wherein V is selected from the group of aryl and substituted aryl.

83. (Original) A compound according to claim 82 wherein V is selected from the group of phenyl, 3,5-dichlorophenyl, 3-bromo-4-fluorophenyl, 3-chlorophenyl, 2-bromophenyl, and 3-bromophenyl.

84. (Original) A compound according to claim 81 wherein V is selected from the group of heteroaryl and substituted heteroaryl.

85. (Original) A compound according to claim 84 wherein V is 4-pyridyl.

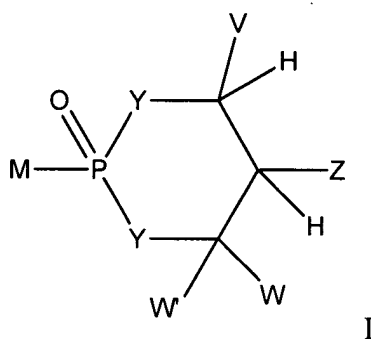
86. (Original) A compound according to claim 81 wherein V is selected from the group of phenyl, phenyl substituted with 1-2 halogens and 4-pyridyl and MH is selected from the group of etoposide, doxorubicin, and taxol.

87. (Original) A compound according to claim 65 wherein MH is from the class epipodophyllotoxins.

88. (Original) A compound according to claim 87 wherein MH is selected from the group of Etoposide, Teniposide, NK-611, GL-331, and Azatoxin.

89.-103. (Withdrawn)

104. (Original) A compound of formula I:



wherein

Z is selected from the group of:

-CHR²OH, -CHR²OC(O)R³, -CHR²OC(S)R³, -CHR²OCO₂R³, -CHR²OC(O)SR³,
-CHR²OC(S)OR³, -SR², -CH₂aryl, -CH(aryl)OH, -CH(CH=CR²)OH, -CH(C≡CR²)OH; and -
CH₂NHaryl;

V, W and W' are independently selected from the group of -H, alkyl, aralkyl, and alicyclic;

with the provisos that:

a) when Z is CHR²OH, then M is not -NH(lower alkyl), -N(lower alkyl)₂, -
NH(lower alkylhalide), -N(lower alkylhalide)₂ or -N(lower alkyl)(lower alkylhalide);

b) when V is aryl or substituted aryl, then M is not -O(D) where D is hydrogen, a metal ion or an ammonium ion; and

R² is selected from the group of R³ and -H;

R³ is selected from the group of alkyl, aryl, alicyclic, and aralkyl;

R⁶ is selected from the group of -H, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

each Y is independently selected from the group of -O-, and -NR⁶-;

M is selected from the group of drugs MH containing an -OH, -NHR², or -SH group, and that is attached to the phosphorus in formula I via O, N, or S of said OH, -NHR², or SH group;

and pharmaceutically acceptable prodrugs and salts thereof.

105. (Original) A compound according to claim 104 wherein MH is selected from the group of antiviral, anticancer, antihyperlipidemic, anti-inflammatory, antifibrotic, anti-diabetic and antiparasitic agents, with the proviso that said anti-diabetic agent is not an FBPase inhibitor.

106. (Original) A compound according to claim 105 wherein MH is selected from the group of etoposide, teniposide, NK-611, GL-331, camptothecin, irinotecan, 9-aminocamptothecin, GG-211, topotecan, lurtotecan, DX-8951F, SKF 107874, SKF 108025, docetaxel, FCE-28161, paclitaxel, mitoxantrone, combretastatin A-4, Azatoxin, mycophenolic acid, coformycin, deoxycoformycin, S,S-dioxolane Combretastatin A-4, doxorubicin, daunorubicin, idarubicin, epirubicin, pirarubicin, mitomycin, eflornithine, piroxantrone, mitoxantrone, neocarzinostatin, esperamicin, calicheamicin theta, and losoxantrone.

107. (Original) A compound according to claim 106 wherein MH is selected from the group of etoposide, teniposide, doxorubicin, pirarubicin, mitoxantrone, topotecan, irinotecan, combretastatin A-4, S,S-dioxolane combretastatin, neocarzinostatin, and calicheamicin.

108. (Original) A compound according to claim 104 wherein at least one Y group is -O-.

109. (Original) A compound according to claim 108 wherein both Y groups are -O-, or when one Y group is -O-, then it is located closest to the W' and W groups.

110. (Original) A compound according to claim 107 wherein both Y groups are -O-.

111. (Original) A compound according to claim 104 wherein V, W, and W' are -H.

112. (Original) A compound according to claim 104 wherein W and W' are the same group.

113. (Original) A compound according to claim 112 wherein V, W, and W' are H.

114. (Original) A compound according to claim 104 wherein M is attached to phosphorus via an oxygen or nitrogen atom.

115. (Original) A compound according to claim 111 wherein Z is selected from the group of $-\text{CHR}^2\text{OH}$, $-\text{CHR}^2\text{OC}(\text{O})\text{R}^3$, and $-\text{CHR}^2\text{OCO}_2\text{R}^3$, and wherein R^2 is H or aryl.

116. (Original) A compound according to claim 115 wherein R^2 is -H, and Y is -O-.

117. (Original) A compound according to claim 104 wherein MH is from the class epipodophyllotoxins.

118. (Original) A compound according to claim 117 wherein MH is selected from the group of Etoposide, Teniposide, NK-611, GL-331, and Azatoxin.

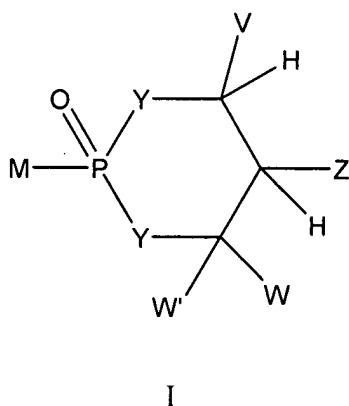
119.-154. (Withdrawn)

155. (Original) A compound according to claim 12, wherein the hydrogen geminal to V and the oxygen attached to the phosphorus via a double bond are in a cis configuration with respect to each other.

156. (Original) A compound according to claim 65, wherein the hydrogen geminal to V and the oxygen attached to the phosphorus via a double bond are in a cis configuration with respect to each other.

157. (Original) A compound according to claim 12 wherein W' and Z are H; W and V are both the same aryl, substituted aryl, heteroaryl, or substituted heteroaryl, and V and W are trans to each other.

158. (Currently amended) A method of treating diseases of the liver or metabolic diseases where the liver is responsible for the overproduction of a biochemical end product by administering to an animal ~~in need thereof~~ a pharmaceutically effective amount of a compound of formula I:



wherein:

V, W, and W' are independently selected from the group of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxy carbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group of $-\text{CHR}^2\text{OH}$, $-\text{CHR}^2\text{OC}(\text{O})\text{R}^3$, $-\text{HR}^2\text{OC}(\text{S})\text{R}^3$, $-\text{CHR}^2\text{OC}(\text{S})\text{OR}^3$, $-\text{CHR}^2\text{OC}(\text{O})\text{SR}^3$, $-\text{CHR}^2\text{OCO}_2\text{R}^3$, $-\text{OR}^2$, $-\text{SR}^2$, $-\text{CHR}^2\text{N}_3$, $-\text{CH}_2\text{aryl}$, $-\text{CH}(\text{aryl})\text{OH}$, $-\text{CH}(\text{CH}=\text{CR}^2_2)\text{OH}$, $-\text{CH}(\text{C}\equiv\text{CR}^2_2)\text{OH}$, $-\text{R}^2$, $-\text{NR}^2_2$, $-\text{OCOR}^3$, $-\text{OCO}_2\text{R}^3$, $-\text{SCOR}^3$, SCO_2R^3 , $-\text{NHCOR}^2$, $-\text{NHCO}_2\text{R}^3$, $-\text{CH}_2\text{NHaryl}$, $-(\text{CH}_2)_p-\text{OR}^{12}$, and $-(\text{CH}_2)_p-\text{SR}^{12}$;

p is an integer 2 or 3;

with the provisos that:

- a) V, Z, W, W' are not all -H;
- b) when Z is $-\text{R}^2$ or $-\text{OR}^2$, then V is not -H, alkyl, aralkyl, or alicyclic;
- c) when Z is CHR^2OH , then M is not $-\text{NH}(\text{lower alkyl})$, $-\text{N}(\text{lower alkyl})_2$, $-\text{NH}(\text{lower alkylhalide})$, $-\text{N}(\text{lower alkylhalide})_2$ or $-\text{N}(\text{lower alkyl})(\text{lower alkylhalide})$; and
- d) when V is aryl or substituted aryl, then M is not $-\text{O}(\text{D})$ where D is hydrogen, a metal ion or an ammonium ion;

R^2 is selected from the group of R^3 and -H;

R^3 is selected from the group of alkyl, aryl, alicyclic, and aralkyl;

R^6 is selected from the group of -H, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

R^{12} is selected from the group of -H, and lower acyl;

each Y is independently selected from the group of -O-, and $-\text{NR}^6$ -;

M is selected from the group of drugs MH containing an -OH , -NHR^2 , or -SH group, and that is attached to the phosphorus in formula I via O, N or S of said OH, -NHR^2 , or -SH group; and pharmaceutically acceptable prodrugs and salts thereof.